STN - structure Search 9-21-05

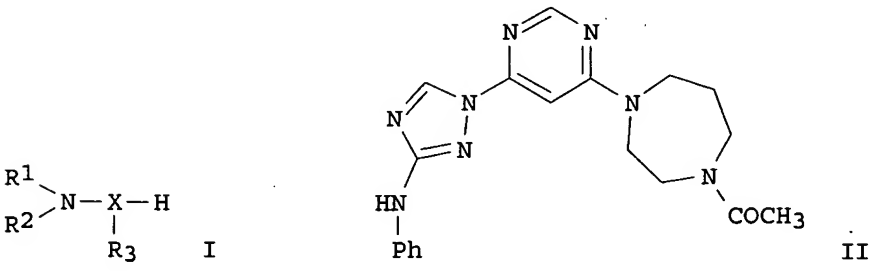
=> d ibib abs hitstr 1-2

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:136554 CAPLUS
DOCUMENT NUMBER: 142:240435
TITLE: Preparation of aminotriazole compounds useful as inhibitors of protein kinases
INVENTOR(S): Davies, Robert J.; Arnost, Michael J.; Bemis, Guy W.; Forster, Cornelia J.; Grey, Ronald, Jr.; Ledford, Brian; Marhefka, Craig; Messersmith, David; Pierce, Albert C.; Salituro, Francesco; Wang, Jian
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA; Ledeboer, Mark W.
SOURCE: PCT Int. Appl., 190 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005013982	A1	20050217	WO 2004-US25539	20040806

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-492787P P 20030806
OTHER SOURCE(S): MARPAT 142:240435
GI



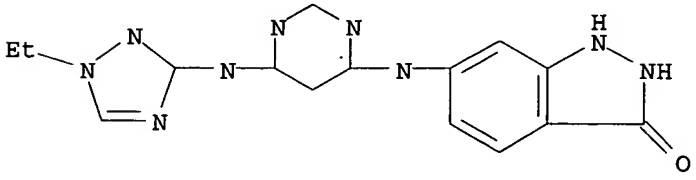
AB Title compds. I [X = 1,2,4-triazolyl; R1 = H or alkyl; R2 = alkyl, arylalkyl, heterocyclicalkyl, etc.; or R1 and R2 together with the N form an (un)substituted heterocyclyl or heteroaryl ring; R3 = alkyl, arylalkyl, heterocyclicalkyl, etc.], and their pharmaceutically acceptable salts, are prepared and disclosed as inhibitors of protein kinases. Thus, e.g., II, was prepared by substitution of 1-(6-chloropyrimidin-4-yl)-3-phenylamino-1H-[1,2,4]triazole (preparation given) with N-acetylhomopiperazine. I were tested vs. numerous kinases for their inhibitory activity, e.g., selected compds. of I possessed IC50 values of < than 0.1 μM against FLT-3. The invention also provides pharmaceutical compns. comprising the compds. of the invention, processes for preparing the compds. and methods of using the

compns. in the treatment of various disorders.

IT **844889-13-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of aminotriazoles with protein kinase inhibitory activity)

RN 844889-13-0 CAPLUS

CN 3H-Indazol-3-one, 6-[[6-[(1-ethyl-1H-1,2,4-triazol-3-yl)amino]-4-pyrimidinyl]amino]-1,2-dihydro- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Inventor?

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:370926 CAPLUS

DOCUMENT NUMBER: 140:391292

TITLE: Preparation of indazolinone compositions useful as kinase inhibitors

INVENTOR(S): Aronov, Alex; Lauffer, David J.; Li, Huan Qui; Tomlinson, Ronald Charles; Li, Pan

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 260 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

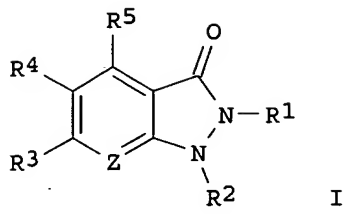
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004037814	A1	20040506	WO 2003-US34065	20031027
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004167121	A1	20040826	US 2003-694534	20031027
PRIORITY APPLN. INFO.:			US 2002-421398P P	20021025

OTHER SOURCE(S): MARPAT 140:391292

GI



I

AB The present invention provides compds. of formula (I). [Wherein R1, R2 = H or a nitrogen protecting group; one of R3 or R4 = R and the other one of R3 or R4 = -Q1-A-Q2-Y; wherein Q1 = a valence bond, NRa, C(Ra)2, S, O, SO2, NRaSO2, SO2NRa, CO, NRaCO, CONRa, OC(O), C(O)O, OC(O)NRa, 1,2-cyclopropanedilyl, 1,2-cyclobutanediyl, or 1,3-cyclobutanediyl, optionally substituted C2-4 alkylidene, etc.; wherein Ra = H, each optionally substituted C1-4 aliphatic; A = optionally substituted 5-to 7-membered monocyclic or 8- to 10-membered bicyclic aryl, heteroaryl, heterocyclic, carbocyclic ring, or C2-6 alkylidene, etc.; Q2 = NRc, SO, O, or C(Rc)2; wherein Rc = H, optionally substituted C1-4 aliphatic; Y = each optionally substituted 5- to 7-membered monocyclic or 8- to 10 membered bicyclic aryl, heteroaryl, heterocyclic, or carbocyclic ring; R5 = R; Z = N, CR6; wherein R6 = R; R = H, halo, Q-halogen, cyano, Q-CN, NO2, Q-NO2, R7, Q-R7; Q = optionally substituted C1-4 alkylidene; wherein one or more methylene units of Q is optionally replaced by O, S, NR7, NR7CO, NR7CONR7, NR7CO2, CO, CO2, CONR7, OC(O)NR7, SO2, SO2NR7, NR7SO2, NR7SO2NR7, C(O)C(O), or C(O)C(R7)2C(O); wherein R7 = H, each optionally substituted aliphatic, heteroaliph., aryl or heteroaryl]. The compds. I and pharmaceutically acceptable compns. thereof, are useful generally as protein kinase inhibitors, particularly as inhibitors of protein kinase PRAK, protein kinase GSK3, protein kinase ERK2, protein kinase CDK2, MAP kinase-activated protein kinase 2 (MK2), SRC kinase, protein kinase SYK, and protein kinase Aurora-2. Accordingly, the compds. I and compns. of the invention are useful for treating or lessening the severity of a disease or condition selected from cardiovascular disease, diabetes, neurol. disorders (e.g. Alzheimer's disease), immunodeficiency disorders, inflammatory diseases, allergic diseases, autoimmune diseases, destructive bone disorders such as osteoporosis, proliferative disorders, infectious diseases, and viral diseases. Thus, a solution of (2-chloroquinazolin-4-yl)(5-cyclopropyl-1H-pyrazol-3-yl)amine (50.0 mg, 0.175 mmol) and 6-amino-3-oxo-2,3-dihydroindazole-1-carboxylic acid tert-Bu ester (69.8 mg. 0.280 mmol) in NMP (1.0 mL) was heated up to 100° for 6 h to give, after workup, acidification with CF3CO2H, and HPLC purification, 6-[[4-[(5-cclopropyl-1H-pyrazol-3-yl)amino]quinazolin-2-yl]amino]-1,2-dihydroindazol-3-one trifluoroacetate. Some compds. of the formula I were shown to have Ki of <0.1 μM for GSK-3 and Aurora-2 and <1.0 μM for CDK-2, ERK2, PRAK, SRC, SYK, and MK2.

IT **685866-54-0P**

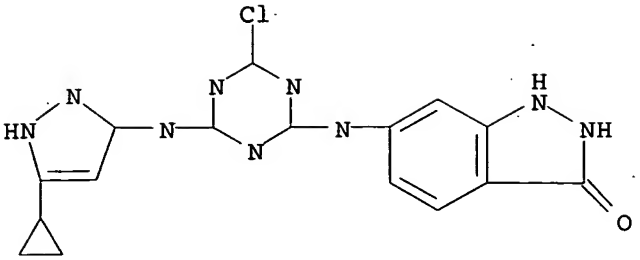
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(intermediate; preparation of indazolinone derivs. as kinase inhibitors for treating or lessening severity of diseases or conditions)

RN 685866-54-0 CAPLUS

CN 3H-Indazol-3-one, 6-[[4-[(5-cyclopropyl-1H-pyrazol-3-yl)amino]-2-quinazolinyl]amino]-1,2-dihydro-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

CRN 685866-53-9
CMF C21 H18 N8 O



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

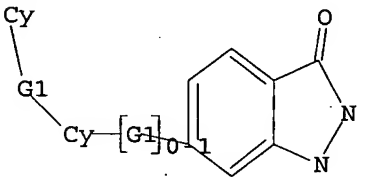
=> d his

(FILE 'HOME' ENTERED AT 09:58:51 ON 21 SEP 2005)

FILE 'REGISTRY' ENTERED AT 09:59:04 ON 21 SEP 2005
L1 STRUCTURE UPLOADED
L2 2 S L1
L3 48 S L1 FULL

FILE 'CAPLUS' ENTERED AT 09:59:40 ON 21 SEP 2005
L4 2 S L3

=> d l1
L1 HAS NO ANSWERS
L1 STR



G1 C,O,S,N

Structure attributes must be viewed using STN Express query preparation.

=> => d ibib abs hitstr 1-5

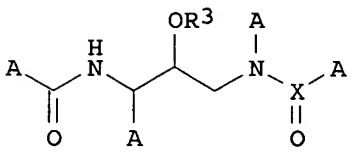
L4 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:612479 CAPLUS
DOCUMENT NUMBER: 143:97530
TITLE: Preparation of phosphonate analogs of HIV protease inhibitors and methods for identifying anti-HIV therapeutic compounds
INVENTOR(S): Arimilli, Murty N.; Becker, Mark M.; Birkus, Gabriel; Bryant, Clifford; Chen, James M.; Chen, Xiaowu; Cihlar, Tomas; Dastgah, Azar; Eisenberg, Eugene J.; Fardis, Maria; Hatada, Marcos; He, Gong-Xin; Jin, Haolun; Kim, Choung U.; Lee, William A.; Lee, Christopher P.; Lin, Kuei-Ying; Liu, Hongtao; Mackman, Richard L.; McDermott, Martin J.; Mitchell, Michael L.; Nelson, Peter H.; Pyun, Hyung-Jung; Rowe, Tanisha D.; Sparacino, Mark; Swaminathan, Sundaramoorthi; Tario, James D.; Wang, Jianying; Williams, Matthew A.; Xu, Lianhong; Yang, Zheng-Yu; Yu, Richard H.; Zhang,

Jiancun; Zhang, Lijun
PATENT ASSIGNEE(S): Gilead Sciences, Inc., USA
SOURCE: PCT Int. Appl., 1723 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

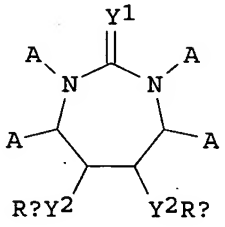
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005064008	A1	20050714	WO 2004-US42991	20041222

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

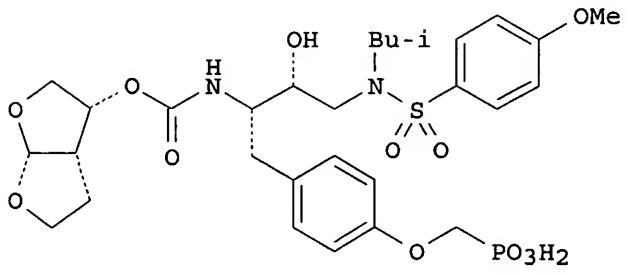
PRIORITY APPLN. INFO.: US 2003-740694 A 20031222
GI



I



II



III

AB The invention relates to phosphonate-substituted carbamates I and cyclic ureas II [wherein A = A1, A2, or W3 with the proviso that at least one of A = A1; A1 = [Y2(CR2R2)1-12]0-12Y2W6; A2 = [Y2(CR2R2)1-12]0-12Y2W3; W3 = substituted (hetero)cyclyl, R5, C(Y1)R5, C(Y1)W5, SO2R5, or SO2W5; W5 = substituted (hetero)cyclyl; W6 = triphosphono-substituted W3; Y1 = O, S, N(Rx), N(O)(Rx), N(ORx), N(O)(ORx), or N(N(Rx)2); Y2 = independently a bond, O, N(Rx), N(O)(Rx), N(ORx), N(O)(ORx), N(N(Rx)2), SO0-2, or SO0-2SO0-2; Rx = independently H, R1, W3, a protecting group, etc.; R1 = independently H or alkyl; R2 = independently H, R1, halo, CN, N3, NO2, Y1, Rx, N(Rx)2, S0-2Rx, substituted alkyl, alkenyl, alkynyl, etc.; R3 = halo, CN, N3, NO2, Y1, Rx, N(Rx)2, SRx, SORx, SO2Rx, OC(Y1)Rx, OC(Y1)ORx,

C(Y1)Rx, etc. with provisos; R5 = substituted alkyl, alkenyl, or alkynyl; or pharmaceutically acceptable salts, hydrates, and formulations thereof] and other phosphonate-substituted analogs of HIV protease inhibitors for treating AIDS and other antiviral infections, as well as for use in assays for the detection of HIV protease. Compds. of the invention inhibit reverse transcriptase activity and have improved intracellular half-life compared to analogs not having the phosphonate or phosphonate prodrug. Libraries of such compds. were screened optionally using the novel enzyme GS-7340 ester hydrolase. Compns. and methods relating to GS-7340 ester hydrolase also are provided. Examples include prepns. for non-nucleoside phosphonate protease inhibitors. In addition, extensive biol. data regarding PBMC uptake and metabolism, serum stability, and alkaline phosphatase protease inhibitor (ALPPI) activity of selected phosphonate-substituted prodrugs is presented. For instance, a 9-step reaction sequence starting from N-tert-butoxycarbonyl-O-benzyl-L-tyrosine provided III (Ki ≤10 pM for ALPPI activity). The synthesis involved multiple protection and deprotection steps along with coupling reactions using isobutylamine, (3R,3aR,6aS)-hexahydrofuro[2,3-b]furan-2-yl 4-nitrophenyl carbonate, and dibenzyl hydroxymethylphosphonate.

IT **622872-39-3P 622872-41-7P**

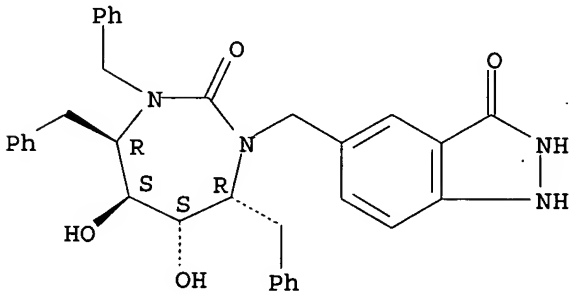
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(protease inhibitor; preparation of phosphonate-substituted HIV protease inhibitors for treatment of AIDS and other viral infections)

RN 622872-39-3 CAPLUS

CN 3H-Indazol-3-one, 5-[[(4R,5S,6S,7R)-hexahydro-5,6-dihydroxy-2-oxo-3,4,7-tris(phenylmethyl)-1H-1,3-diazepin-1-yl]methyl]-1,2-dihydro- (9CI) (CA INDEX NAME)

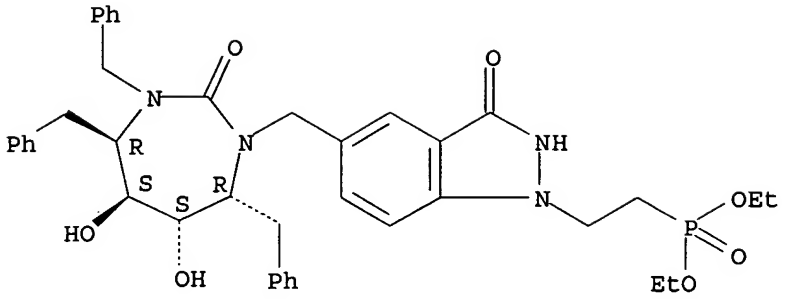
Absolute stereochemistry.



RN 622872-41-7 CAPLUS

CN Phosphonic acid, [2-[5-[[(4R,5S,6S,7R)-hexahydro-5,6-dihydroxy-2-oxo-3,4,7-tris(phenylmethyl)-1H-1,3-diazepin-1-yl]methyl]-2,3-dihydro-3-oxo-1H-indazol-1-yl]ethyl]-, diethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:158622 CAPLUS
DOCUMENT NUMBER: 142:279952
TITLE: Preparation of aralkanoates as inhibitors of prostaglandin and leukotriene production.
INVENTOR(S): Shoda, Motoshi; Kuriyama, Hiroshi
PATENT ASSIGNEE(S): Asahi Kasei Pharma Corporation, Japan
SOURCE: PCT Int. Appl., 687 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005016862	A1	20050224	WO 2004-JP11952	20040813
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2005016862	A1	20050224	WO 2004-XA11952	20040813
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2005016862	A1	20050224	WO 2004-XB11952	20040813
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ,				

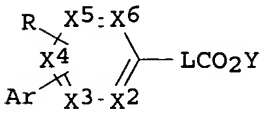
TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

WO 2005016862 A1 20050224 WO 2004-XC11952 20040813
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:
JP 2003-293590 A 20030814
US 2003-495734P P 20030818
WO 2004-JP11952 A 20040813

OTHER SOURCE(S): MARPAT 142:279952

GI



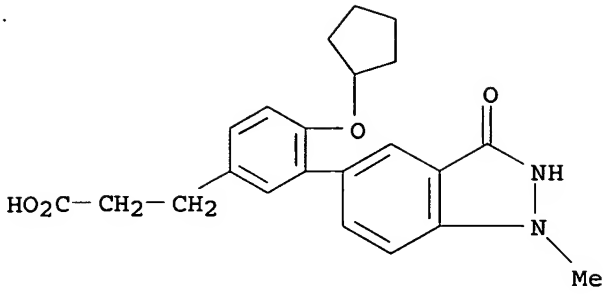
I

AB Title compds. [I; L = (unsatd.) C1-3 hydrocarbon chain; X2-X6 = CH, V; ≤1 of X2-X6 = V; V = N, CZ; Z = alkyl, F, Cl, Br, OH, alkoxy, amino, etc.; R = DRx, amino;, D = bond, O, S, SO, SO2, CO; Rx = alkyl, aminoalkyl, etc.; Ar = (substituted) partially or completely unsatd. condensed carbobicyclyl, heterocyclyl; Y = H, alkyl, aminoalkyl, etc.], were prepared Thus, Me 3-[4-cyclopentyloxy-3-(naphthalen-2-yl)phenyl]propionate (preparation outlined) and other I inhibited IL-1β induced PGE2 production by ≥50% at 1.0 μM. [This abstract record is one of 4 records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.].

IT **847066-19-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aralkanoates as inhibitors of prostaglandin and leukotriene production)

RN 847066-19-7 CAPLUS

CN Benzenepropanoic acid, 4-(cyclopentyloxy)-3-(2,3-dihydro-1-methyl-3-oxo-1H-indazol-5-yl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

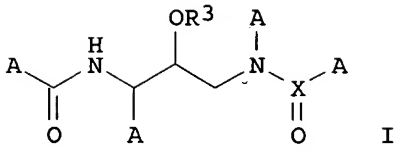
L4 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:875072 CAPLUS
DOCUMENT NUMBER: 139:381610
TITLE: Preparation of phosphonate analogs of HIV protease inhibitors and methods for identifying anti-HIV therapeutic compounds
INVENTOR(S): Birkus, Gabriel; Chen, James M.; Chen, Xiaowu; Cihlar, Tomas; Eisenberg, Eugene J.; Hatada, Marcos; He, Gong-Xin; Kim, Choung U.; Lee, William A.; McDermott, Martin J.; Swaminathan, Sundaramoorthi
PATENT ASSIGNEE(S): Gilead Sciences, Inc., USA
SOURCE: PCT Int. Appl., 814 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003090691	A2	20031106	WO 2003-US12943	20030425
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2481449	AA	20031106	CA 2003-2481449	20030425
US 2004121316	A1	20040624	US 2003-424186	20030425
US 2005197320	A1	20050908	US 2003-424130	20030425
WO 2004096818	A2	20041111	WO 2003-EP12423	20031106
WO 2004096818	A3	20050407		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005136397	A1	20050623	US 2004-970389	20041022

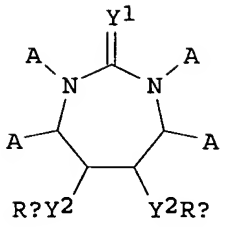
PRIORITY APPLN. INFO.:

US 2002-375622P	P	20020426
US 2002-375665P	P	20020426
US 2002-375779P	P	20020426
US 2002-375834P	P	20020426
WO 2003-US12901	A	20030425
WO 2003-US12926	A	20030425
WO 2003-US12943	W	20030425
US 2003-513532P	P	20031024
US 2003-513542P	P	20031024
US 2003-514241P	P	20031024
US 2003-514299P	P	20031024
US 2003-514894P	P	20031029
US 2003-514925P	P	20031029
WO 2004-US35083	A	20041022

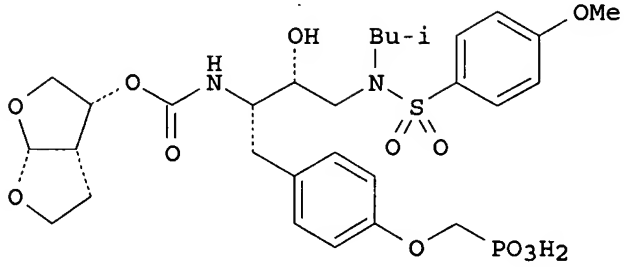
GI



I



II



III

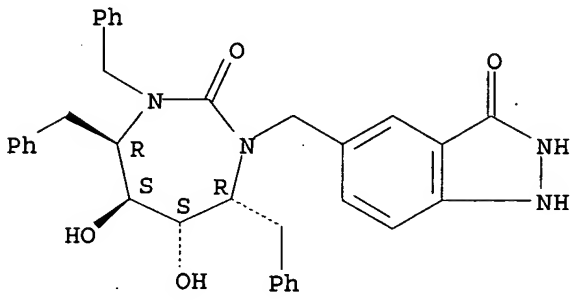
AB The invention relates to phosphonate-substituted carbamates I and cyclic ureas II [wherein A = A1, A2, or W3 with the proviso that at least one of A = A1; A1 = [Y2(CR2R2)1-12]0-12Y2W6; A2 = [Y2(CR2R2)1-12]0-12Y2W3; W3 = substituted (hetero)cyclyl, R5, C(Y1)R5, C(Y1)W5, SO2R5, or SO2W5; W5 = substituted (hetero)cyclyl; W6 = triphosphono-substituted W3; Y1 = O, S, N(Rx), N(O)(Rx), N(ORx), N(O)(ORx), or N(N(Rx)2); Y2 = independently a bond, O, N(Rx), N(O)(Rx), N(ORx), N(O)(ORx), N(N(Rx)2), SO0-2, or SO0-2SO0-2; Rx = independently H, R1, W3, a protecting group, etc.; R1 = independently H or alkyl; R2 = independently H, R1, halo, CN, N3, NO2, Y1, Rx, N(Rx)2, S0-2Rx, substituted alkyl, alkenyl, alkynyl, etc.; R3 = halo, CN, N3, NO2, Y1, Rx, N(Rx)2, SRx, SORx, SO2Rx, OC(Y1)Rx, OC(Y1)ORx, C(Y1)Rx, etc. with provisos; R5 = substituted alkyl, alkenyl, or alkynyl; or pharmaceutically acceptable salts, hydrates, and formulations thereof] and other phosphonate-substituted analogs of HIV protease inhibitors for treating AIDS and other antiviral infections, as well as for use in assays for the detection of HIV protease. Compds. of the invention inhibit reverse transcriptase activity and have improved intracellular half-life compared to analogs not having the phosphonate or phosphonate prodrug. Libraries of such compds. were screened optionally using the novel enzyme GS-7340 ester hydrolase. Compns. and methods relating to GS-7340 ester hydrolase also are provided. Examples include prepns. for non-nucleoside

phosphonate protease inhibitors. In addition, extensive biol. data regarding PBMC uptake and metabolism, serum stability, and alkaline phosphatase protease inhibitor (ALPPI) activity of selected phosphonate-substituted prodrugs is presented. For instance, a 9-step reaction sequence starting from N-tert-butoxycarbonyl-O-benzyl-L-tyrosine provided III (Ki ≤10 pM for ALPPI activity). The synthesis involved multiple protection and deprotection steps along with coupling reactions using isobutylamine, (3R,3aR,6aS)-hexahydrofuro[2,3-b]furan-2-yl 4-nitrophenyl carbonate, and dibenzyl hydroxymethylphosphonate.

IT **622872-39-3P 622872-41-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(protease inhibitor; preparation of phosphonate-substituted HIV protease inhibitors for treatment of AIDS and other viral infections)

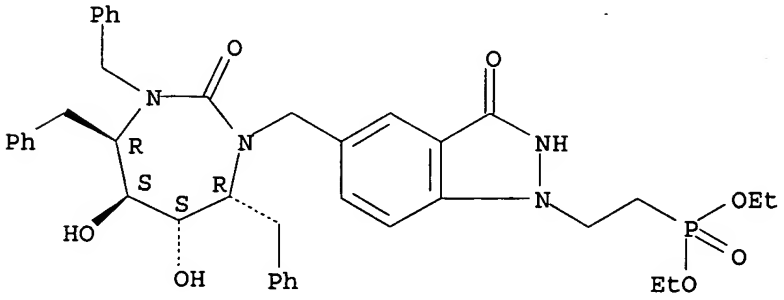
RN 622872-39-3 CAPLUS
CN 3H-Indazol-3-one, 5-[[(4R,5S,6S,7R)-hexahydro-5,6-dihydroxy-2-oxo-3,4,7-tris(phenylmethyl)-1H-1,3-diazepin-1-yl]methyl]-1,2-dihydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 622872-41-7 CAPLUS
CN Phosphonic acid, [2-[5-[[(4R,5S,6S,7R)-hexahydro-5,6-dihydroxy-2-oxo-3,4,7-tris(phenylmethyl)-1H-1,3-diazepin-1-yl]methyl]-2,3-dihydro-3-oxo-1H-indazol-1-yl]ethyl]-, diethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:875071 CAPLUS
DOCUMENT NUMBER: 139:381609
TITLE: Preparation of phosphonate analogs of HIV protease inhibitors with improved cellular accumulation properties
INVENTOR(S): Arimilli, Murty N.; Becker, Mark M.; Bryant, Clifford;

Chen, James M.; Chen, Xiaowu; Dastgah, Azar; Fardis, Maria; He, Gong-Xin; Jin, Haolun; Kim, Choung U.; Lee, William A.; Lee, Christopher P.; Lin, Kuei-Ying; Liu, Hongtao; Mackman, Richard L.; Mitchell, Michael L.; Nelson, Peter H.; Pyun, Hyung-Jung; Rowe, Tanisha D.; Sparacino, Mark; Swaminathan, Sundaramoorthi; Tario, James D.; Wang, Jianying; Williams, Matthew A.; Xu, Lianhong; Yang, Zheng-Yu; Yu, Richard H.; Zhang, Jiancun; Zhang, Lijun

PATENT ASSIGNEE(S): Gilead Sciences, Inc., USA

SOURCE: PCT Int. Appl., 1727 pp.
CODEN: PIXXD2

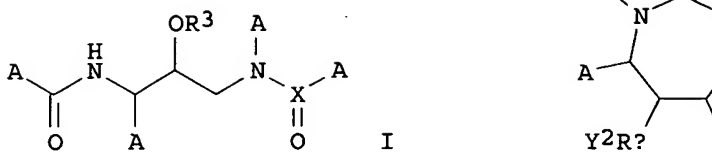
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003090690	A2	20031106	WO 2003-US12901	20030425
WO 2003090690	A3	20040624		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2481261	AA	20031106	CA 2003-2481261	20030425
US 2004121316	A1	20040624	US 2003-424186	20030425
BR 2003009573	A	20050201	BR 2003-9573	20030425
EP 1509537	A2	20050302	EP 2003-747326	20030425
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005523912	T2	20050811	JP 2003-587329	20030425
US 2005197320	A1	20050908	US 2003-424130	20030425
WO 2004096818	A2	20041111	WO 2003-EP12423	20031106
WO 2004096818	A3	20050407		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

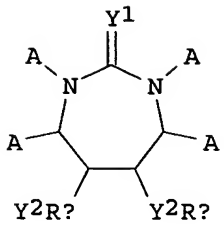
PRIORITY APPLN. INFO.:

US 2002-375622P	P	20020426
US 2002-375665P	P	20020426
US 2002-375779P	P	20020426
US 2002-375834P	P	20020426
WO 2003-US12901	W	20030425
WO 2003-US12926	A	20030425
WO 2003-US12943	A	20030425

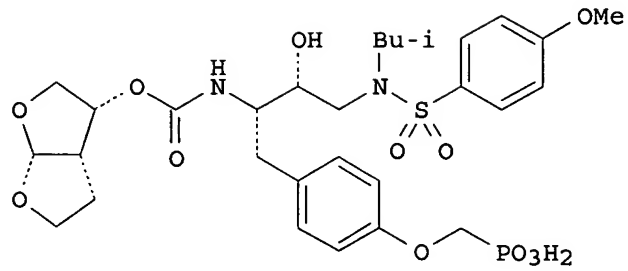
OTHER SOURCE(S): MARPAT 139:381609
GI



I



II



III

AB The invention relates to phosphonate-substituted carbamates I and cyclic ureas II [wherein A = A1, A2, or W3 with the proviso that at least one of A = A1; A1 = [Y2(CR2R2)1-12]0-12Y2W6; A2 = [Y2(CR2R2)1-12]0-12Y2W3; W3 = substituted (hetero)cyclyl, R5, C(Y1)R5, C(Y1)W5, SO2R5, or SO2W5; W5 = substituted (hetero)cyclyl; W6 = triphosphono-substituted W3; Y1 = O, S, N(Rx), N(O)(Rx), N(ORx), N(O)(ORx), or N(N(Rx)2); Y2 = independently a bond, O, N(Rx), N(O)(Rx), N(ORx), N(O)(ORx), N(N(Rx)2), SO0-2, or SO0-2SO0-2; Rx = independently H, R1, W3, a protecting group, etc.; R1 = independently H or alkyl; R2 = independently H, R1, halo, CN, N3, NO2, Y1, Rx, N(Rx)2, S0-2Rx, substituted alkyl, alkenyl, alkynyl, etc.; R3 = halo, CN, N3, NO2, Y1, Rx, N(Rx)2, SRx, SORx, SO2Rx, OC(Y1)Rx, OC(Y1)ORx, C(Y1)Rx, etc. with provisos; R5 = substituted alkyl, alkenyl, or alkynyl; or pharmaceutically acceptable salts, hydrates, and formulations thereof] and other phosphonate-substituted analogs of HIV protease inhibitors for treating AIDS and other antiviral infections, as well as for use in assays for the detection of HIV protease. Compds. of the invention inhibit reverse transcriptase activity and have improved intracellular half-life compared to analogs not having the phosphonate or phosphonate prodrug. Examples include prepns. for non-nucleoside saquinavir-like, lopinavir-like, ritonavir-like, indinavir-like, atazanavir-like, nefinavir-like, tipranavir-like, amprenavir-like, KNI-like, and cyclic carbonyl-like phosphonate protease inhibitors. In addition, extensive biol. data regarding PBMC uptake and metabolism, serum stability, and alkaline phosphatase protease inhibitor (ALPPI) activity of selected phosphonate-substituted prodrugs is presented. For instance, a 9-step reaction sequence starting from N-tert-butoxycarbonyl-O-benzyl-L-tyrosine provided III (Ki ≤10 pM for ALPPI activity). The synthesis involved multiple protection and deprotection steps along with coupling reactions using isobutylamine, (3R,3aR;6aS)-hexahydrofuro[2,3-b]furan-2-yl 4-nitrophenyl carbonate, and dibenzyl hydroxymethylphosphonate.

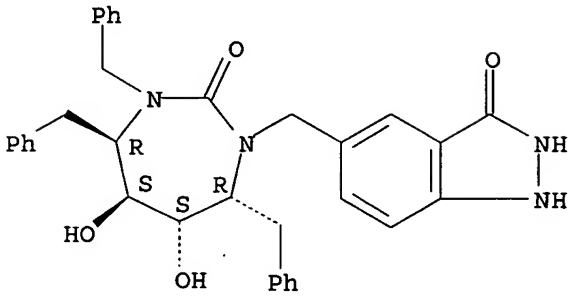
IT **622872-39-3P 622872-41-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(protease inhibitor; preparation of phosphonate-substituted HIV protease inhibitors for treatment of AIDS and other viral infections)

RN 622872-39-3 CAPLUS

CN 3H-Indazol-3-one, 5-[[(4R,5S,6S,7R)-hexahydro-5,6-dihydroxy-2-oxo-3,4,7-tris(phenylmethyl)-1H-1,3-diazepin-1-yl]methyl]-1,2-dihydro- (9CI) (CA

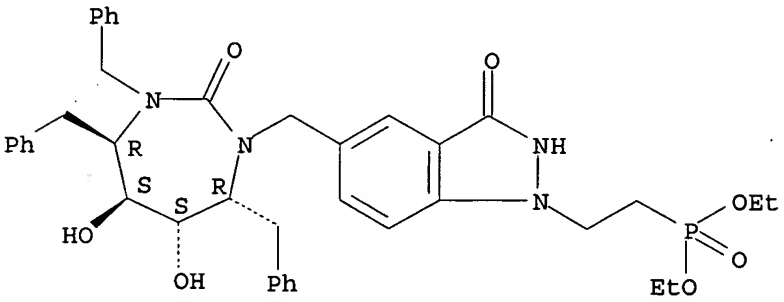
INDEX NAME)

Absolute stereochemistry.

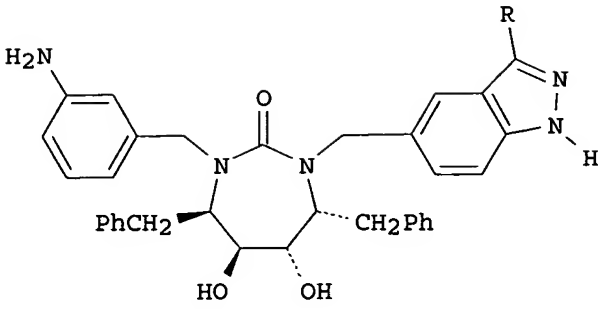


RN 622872-41-7 CAPLUS
CN Phosphonic acid, [2-[5-[[(4R,5S,6S,7R)-hexahydro-5,6-dihydroxy-2-oxo-3,4,7-tris(phenylmethyl)-1H-1,3-diazepin-1-yl]methyl]-2,3-dihydro-3-oxo-1H-indazol-1-yl]ethyl]-, diethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:769083 CAPLUS
DOCUMENT NUMBER: 132:122591
TITLE: Unsymmetrical cyclic ureas as HIV-1 protease inhibitors: novel biaryl indazoles as P2/P2' substituents
AUTHOR(S): Patel, Mona; Rodgers, James D.; McHugh, Robert J., Jr.; Johnson, Barry L.; Cordova, Beverly C.; Klabe, Ronald M.; Bacheler, Lee T.; Erickson-Viitanen, Susan; Ko, Soo S.
CORPORATE SOURCE: DuPont Pharmaceuticals Company, Wilmington, DE, 19880-0500, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (1999), 9(22), 3217-3220
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 132:122591
GI



I

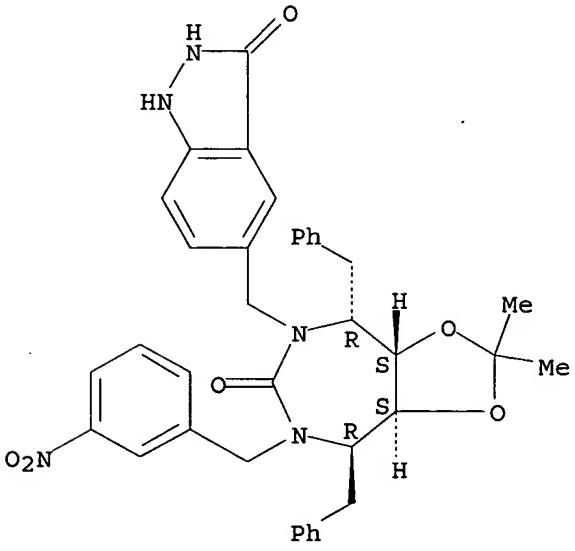
AB The preparation of unsym. cyclic ureas bearing novel biaryl indazoles as P2/P2' substituents was undertaken, utilizing a Suzuki coupling reaction as the key step. Compound I (R = 4-MeOC6H4) was equipotent to the lead compound of the series SE063 I (R = H).

IT **256345-53-6P 256345-54-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and biol. activity of indazolylmethyldiazepinones as HIV-1 protease inhibitors)

RN 256345-53-6 CAPLUS

CN 6H-1,3-Dioxolo[4,5-e][1,3]diazepin-6-one, 5-[(2,3-dihydro-3-oxo-1H-indazol-5-yl)methyl]hexahydro-2,2-dimethyl-7-[(3-nitrophenyl)methyl]-4,8-bis(phenylmethyl)-, (3aS,4R,8R,8aS)- (9CI) (CA INDEX NAME)

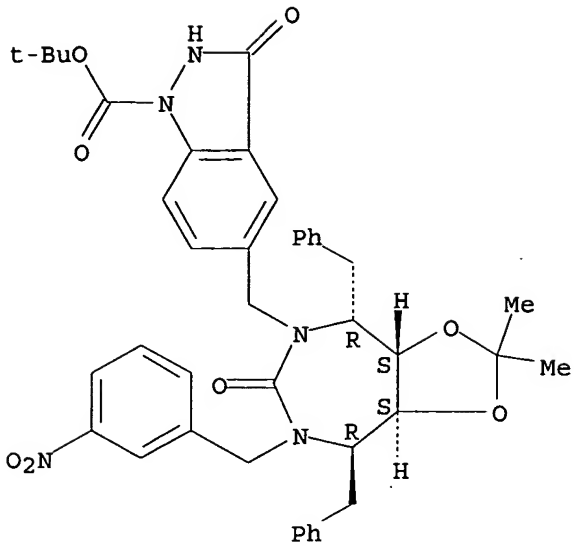
Absolute stereochemistry.



RN 256345-54-7 CAPLUS

CN 1H-Indazole-1-carboxylic acid, 5-[[(3aS,4R,8R,8aS)-hexahydro-2,2-dimethyl-7-[(3-nitrophenyl)methyl]-6-oxo-4,8-bis(phenylmethyl)-5H-1,3-dioxolo[4,5-e][1,3]diazepin-5-yl]methyl]-2,3-dihydro-3-oxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

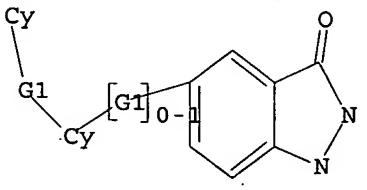
=> d his

(FILE 'HOME' ENTERED AT 10:03:54 ON 21 SEP 2005)

FILE 'REGISTRY' ENTERED AT 10:04:05 ON 21 SEP 2005
L1 STRUCTURE UPLOADED
L2 0 S L1
L3 5 S L1 FULL

FILE 'CAPLUS' ENTERED AT 10:04:42 ON 21 SEP 2005
L4 5 S L3

=> d l1
L1 HAS NO ANSWERS
L1 STR



G1 C,O,S,N

Structure attributes must be viewed using STN Express query preparation.

=>